REMARKS

THE INVENTION

This invention provides for the administration of an anti-neoplastic drug:carrier complex to generate a humoral response to the anti-neoplastic drug in a patient who will be subsequently treated with the drug. The antibodies are expected to reduce the toxicity of the drug by moderating delivery of drug to the sites of toxicity. Modernly, this approach to cancer treatment is called, "inverse targeting strategies."

STATUS OF THE CLAIMS

Claims 1, 4, 6, 9, and 12-15 are pending and examined. All claims are rejected under 35 U.S.C. §112, first paragraph as non-enabled.

REJECTIONS

There is a single rejection of the pending claims. The pending claims are all rejected under 35 U.S.C. §112 as non-enabled. The Examiner writes that administration of anti-neoplastic drugs conjugated to a carrier would be expected to give rise to a humoral response; but, then argues that the antibodies would prevent the anti-neoplastic drugs from reaching their intended target. The Examiner writes on page 3 of the Office Action:

> The specification does not address how to provide a pre-existing humoral immune response wherein the said humoral response would not interfere with the desired anti-neoplastic effect of said compound.

The pending claims are directed to anti-neoplastic drugs and are intended to be used in the same manner as the anti-cocaine claims previously issued to the inventor in the parent application, now U.S. Pat. No. 6,210,677.

The generic invention disclosed in the application is a method to prevent systemic toxicity via binding and controlled release of toxins by circulating antibodies. In the case of cocaine, the drug is self-administered locally by the drug abusers themselves to nasal mucosa or lung tissue. The antibodies in the circulatory system act as blocking agents to prevent the drug from reaching receptors in the brain or heart in toxic amounts.

In the case of the anti-neoplastic agents, the drugs are administered by doctors locally and the antibodies are expected to prevent systemic toxicity through binding. That is a simple articulation of the invention. As the Examiner may know, there is an equilibrium state created between free antigens and those bound to antibodies. This is not particularly relevant for drugs of abuse where the drug has no beneficial purpose. However, for anti-neoplastic drugs, the equilibrium is expected to have a benefit to the patient. The laws of equilibrium should have a moderating effect on the rate of delivery to the target tissues. Delivery of drug should be more constant over a longer period as the drug is initially complexed to antibody and is then released over time as the free drug is either metabolized or used by the target tissues. For as the free drug disappears, the laws of equilibrium drive the release of more free drug from the antibody:drug complex.

Modernly, scientists working with the applicants' invention call this approach "inverse targeting strategies." Using passive immunotherapy, in contrast to the applicant's claims to active immunotherapy, Lobo and Balthasar (Exhibits 1 and 2) used anti-methotrexate antibodies (anti-MTX) to enhance pharmacokinetic selectivity of intraperitoneal methotrexate therapy in a murine model of peritoneal cancer. They wrote in Exhibit 1 at page 191:

> Traditional drug targeting approaches attempt to enhance the selectivity of drug action by increasing the efficiency of drug action by increasing the drug delivery to desired sites of drug activity. Conversely, **inverse targeting strategies** attempt to increase selectivity by reducing the efficiency of drug delivery to sites associated with drug toxicity.

The Examiner's rejection under §112 presumes that the expected humoral response will prevent all drug from the target tissue and that those of skill would require undue experimentation to practice the invention in a manner that benefits the patient.

As explained above, neither premise is true.

- Antibody:antigen complexing is based on equilibrium laws requiring that a portion of the drug is in the free form and available for the target tissue.
- The invention has obvious applications to local administration of anti-neoplastic drug which is well within the skills of oncologists.
- With regard to systemic drug delivery, the equilibrium between free and antibody complexed anti-neoplastic drug will afford benefit to the patient in moderating rate of delivery of drug to sites of toxicity.

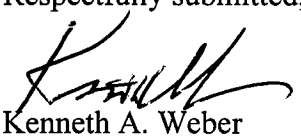
Applicant submits that there is little else to teach for this invention. Both the generation of humoral response and administration of anti-neoplastic drugs are well known. There is no reason to doubt that those of skill can, without undue experimentation, reduce the amount of drug reaching sites of toxicity while affording *some* benefit to the patient from the free drug.

The law of enablement merely requires that patent applicants teach how to make the invention work without undue experimentation. The law does not require that the patent specification teach those of skill how to obtain *optimal* or even *safe* results. Having explained that there will always be some free drug in the body and available to the target cancer cells, the logical basis for the enablement rejection, i.e., that no drug will be available, is fully rebutted.

Applicant believes that all the outstanding concerns raised by the Examiner have been addressed and that the claims are in condition for allowance.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned attorney at (415) 273-4714.

Respectfully submitted,



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Attachments: Exhibits 1 and 2

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